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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,596	02/09/2001	Jean-Richard Neeser	88265-406	6562

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EXAMINER
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ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/779,596	NEESER ET AL.
Examiner	Art Unit	
Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 02 October 2002.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-10 and 23-28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-4, 6-10 and 23-28 is/are rejected.

7) Claim(s) 5 is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. ____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____ .
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5. 6) Other: _____

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 8, mailed on September 12, 2002), Applicants filed an election and amendment received on October 2, 2002 (Paper No. 9). Said amendment cancelled Claims 11-22 and added new Claims 23-28 drawn to the elected invention. Thus, Claims 1-10 and 23-28 are pending in the instant Office action and will be examined herein.

Election

2. Applicant's election of Group I, Claims 1-10, in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)). Claims 1-10 and 23-28 are pending in the instant Office action and will be examined herein.

Priority

3. The instant application requests the benefit of priority for the foreign application 98202707.0 filed in Europe on December 8, 1998 in the declaration. However, the instant application does not comply with the rules set out in 35 U.S.C. § 119 (a)-(d): namely, the foreign application was filed more than 12 months before the U.S. filing date and/or a certified copy of the original foreign application has not been filed with the Office. Applicants are requested to comply with these rules, if possible, or withdraw claims to priority benefits. In the instant Office action, the priority date used is that of the parent application, PCT/EP99/05473 filed on July 26, 1999, claimed as a continuation in the transmittal sheet.

Information Disclosure Statement

4. The information disclosure statement filed on February 9, 2001 (Paper No. 5) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy. The Examiner has corrected references AU, AV, AX, and AY; no action is required by Applicants.

Objections to the Specification

5. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. Complete sentences are required. Moreover, the Examiner suggests the inclusion of the full name of the particular species used – *Streptococcus thermophilus*, *Lactococcus lactis* subsp. *lactis*, and *Lactococcus lactis* subsp. *lactis* biovar *diacetylactis*.

6. The specification is objected to for having improper margins. Due to the small top margin and the whole necessary to assemble the application as a file in the Office, the top lines of the specification have been obscured. A substitute specification is required that has the proper margins. See M.P.E.P. § 608.01.

7. The specification is objected to for the following informalities and/or confusions:

- a) On page 1, second paragraph of the Background, the terms “Streptococci, Lactobacilli, and Actynomyces” are improper; the proper terms are ---*Streptococcus*, *Lactobacillus*, and *Actinomyces*---.

- b) On page 5, second full paragraph, “X17390”, “X14490”, and “X53657” are unclear references. Are these GenBank numbers? If so, appropriate reference is required. See M.P.E.P. § 707.05(e) for the acceptable notation of an internet address.
- c) On page 5, near the bottom, and on page 12 near the top, the terms “quark” and “coffee cream” in reference to dairy products are wholly unclear. Definition, as found in the art, is required to clarify the specification.
- d) On page 5, near the middle, page 7, near the top, and page 12, near the middle (2x), the term “renneted milk” is found, but its definition is unclear. Definition, as found in the art, is required to clarify the specification.
- e) On page 14, near the bottom, the term “FUM medium” is noted but the term is unclear. This term is also found in the middle of page 15. Definition, as found in the art, is required to clarify the specification.
- f) On page 15, near the middle, the term “Belliker”, referring to a media, is noted but the term is unclear. Definition, as found in the art, is required to clarify the specification.

Appropriate correction and/or clarification are required for all of the above points.

Objections to the Claims

8. Claim 2 is objected to for an apparent typographical error. The range 5.5 to 5.7 seems quite limited and in the specification on page 6 and again on page 8, the range is 5.5 to 7.0. The claim will be examined as if the range should be 5.5 to 7.0. Appropriate correction and/or clarification are required.

9. Claim 5 is objected to for depending from rejected claims.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-3, 6-10, and 23-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "lactic bacteria that are not part of the resident microflora or the mouth" is unclear as to its exact metes and bounds. Several genera are mentioned in the background section of the specification; however, when particular species are listed (see page 1) only Streptococcus species are listed. The scope of which bacteria are in the mouth is unclear from the specification. Clarification is required.
11. Claims 1-4, 6-10, and 23-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "low acidifying" is a relative term that renders the claim indefinite. The term "low acidifying" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Clarification is required.
12. Claims 2 and 6 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "about" with respect to a pH range or a temperature,

respectively, is unclear as to its metes and bounds. Specifically, it is unclear how varied the pH or temperature can be and still meet the limitations of the claims. Clarification is required.

13. Claim 3 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “of dairy origin” is wholly unclear as to its metes and bounds. Clarification is required.

14. Claim 8 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The reference to gene numbers, as noted above concerning the specification, is wholly unclear. Are these GenBank reference numbers? Perhaps if the specification were clarified on this point, no amendment to the claim may be necessary.

15. Claims 9 and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “milk derivative” is wholly unclear as to its scope. What relatedness to milk is required to be considered a derivative? The metes and bounds of the instant claims are wholly unclear. Clarification is required.

16. Claims 10 and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “renneted milk” is wholly unclear as to its scope.

The definition for the term, as noted above in Objections to the Specification, is wholly unclear.

Clarification is required.

17. Claims 23-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “to provide a pH of at least 5.5” is unclear. Is pH 5.5 a lower limit (so all other numbers meeting the claim’s limitations are more basic) or a higher limit (so all other numbers meeting the claim’s limitations are more acid)? The term is unclear.

Clarification is required.

18. Claims 27-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following terms are unclear as to their definition and/or their metes and bounds: “oil soluble antioxidant”, “abrasive”, “quark”, and “coffee cream”. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claim 28 is rejected under 35 U.S.C. § 132 and 35 U.S.C. § 112, first paragraph, new matter, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

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application was filed, had possession of the claimed invention. The amendment filed on October 2, 2002 adds new matter to Claim 9 as follows: “salad dressing”. On page 12, this list included “sweet salad dressing”, not just salad dressing. Applicant is required to amend the new matter in the reply to this Office Action.

20. Claims 1-4, 6-10, and 23-28 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are directed to dental treatment methods using lactic bacteria where the treatments used in the claimed methods are defined by their functional characteristics (i.e., the ability to adhere to teeth and displace or prevent attachment of other, cariogenic bacteria and be “low acidifying”). The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original).

Just as the claims at issue in UC v. Lilly defined the invention by the function of the claimed DNA (encoding insulin), the instant claims define the claimed methods using products only by their functional properties. The Court held this sort of functional definition insufficient. “In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others

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and can identify many of the species that the claims encompass. Accordingly such a formula is normally an adequate description of the claimed genus. In claims to methods using genetic material, however, a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is" in UC v. Lilly, at *24-*25.

The instant claims are drawn to methods of dental treatment using lactic bacteria having particular characteristics, namely the ability to adhere to teeth and displace or prevent attachment of other, cariogenic bacteria and be "low acidifying". These bacteria were identified in the instant application by a screening process. Applicants have described the five strains in Claim 5, which were borne out of the screening process. No structural commonalities between these strains are defined. The specification does not describe a representative number of species in such a broad genus, except by functional characteristics, because, using only the five described species, one of skill in the art could not reasonably predict the structure of other species encompassed by the claimed genus.

21. Claim 7 is rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using lactic bacteria modified to contain on

of the three genes in Claim 8, does not reasonably provide enablement for methods using lactic bacteria modified in other ways to cause improved adhesion and/or to be less acidifying than the resident microflora. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. To produce the bacteria required for use in the claimed methods would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification presents no guidance of working examples for the production of genetically modified lactic bacteria that have improved adhesion and/or are less acidifying than the resident microflora other than the use of three particular genes as noted in Claim 8. In the absence of any guidance, the quantity of experimentation would be significant. The state of the prior art contains extensive work on mouth microflora, but little is known about genetically modified bacteria that can take up residence in the mouth. Most striking is the unpredictability of the genetic modifications required to meet the limitation of the instant claim to the full extent of its scope. Thus, the instant claim is not enabled to the full extent of its scope.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claims 1-4, 6, 9, and 28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Madinier (WO 92/14475 - see IDS). The instant claims are drawn to methods of treating dental caries in humans or animals by administering *S. thermophilus* or *Lactobacillus* lactic bacteria of dairy origin in a yogurt or milk composition, wherein said bacteria are capable of preventing the adhesion of resident microflora in the mouth. The pH and temperature limitations are unclear in the instant claims; while the bacteria of Madinier may meet these intended limitations, they are not taught.

Madinier teaches *Lactobacillus* and *S. thermophilus* bacterial cultures that “prevent colonization of dental surfaces by e.g. *Streptococcus* mutants”, which are a part of the resident

microflora of the mouth (see Abstract). The cultures can be administered via yogurt and milk (see Abstract).

23. Claims 1-4, 6, and 28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Busscher *et al.* (*Streptococcus thermophilus* and Its Biosurfactants Inhibit Adhesion by *Candida* spp. on Silicone Rubber. *Applied and Environmental Microbiology* (October, 1997) 63(10):3810-3817). The instant claims are drawn to methods of treating dental caries in humans or animals by administering *S. thermophilus* lactic bacteria of dairy origin in a yogurt composition, wherein said bacteria are capable of adhering directly to teeth and displacing or preventing the adhesion of resident microflora in the mouth. The pH and temperature limitations are unclear in the instant claims; while the bacteria of Busscher *et al.* may meet these intended limitations, they are not taught.

Busscher *et al.* teach an adhering *S. thermophilus* B strain found in Turkish yogurt that interferes with yeast adhesion in the oropharynx by virtue of producing a biosurfactant that inhibits adhesion of this yeast that naturally colonizes voice prostheses (see Abstract and page 3812, right column). Culture of the *S. thermophilus* B strain is at 37°C as an optimum (see page 3811, left column).

Other Relevant Art

24. The following is cited for completeness of the record, not having been used in art rejections above:

- a) Van Hoogmoed *et al.* The role of biosurfactants in affecting initial microbial adhesion mechanisms. *Biofilms: Recent Advances in Their Study and Control* (2000) 237-251. Editors: Evans, LV. Publisher: Harwood Academic Publishers, Amsterdam, Neth.

b) USPN 6,03,952 (Oh) teaches mutant *Enterococcus* and *Lactobacillus* strains that degrade plaque; the patent does not teach adherence of the lactic acid bacteria to the teeth.

Conclusion

25. Claim 5 is objected; Claims 1-4, 6-10, and 23-28 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


KMK
December 14, 2002